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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/520,079 | 04/22/2005 | Jamila Najib | BJS-3665-129 | 9192 |
| 23117 7590 04/07/2008 NIXON & VANDERHYE, PC 901 NORTH GLEBE ROAD, 11TH FLOOR ARLINGTON, VA 22203 | | | | |
| EXAMINER | | | | |
| BARKER, MICHAEL P | | | | |
| ART UNIT | | PAPER NUMBER | | |
| 1626 | | | | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/520,079

Applicant(s)

NAJIB ET AL.

Examiner

MICHAEL P. BARKER

Art Unit

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Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01/14/2008, And after Non-Fin.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 69-90, 92-99, 101, 102 and 104-106 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 69-90, 92-99, 101, 102 and 104-106 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 January 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-848)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claims 69-90, 92-99, 101, 102, and 104-106 are pending in this Application.

Response to Remarks

Applicant requests clarification regarding the scope of the subject matter searched. The subject matter was submitted to the PTO's in-house structural search team. From the document titled "Examiner's search strategy and results" (10/01/2007) available in PAIR, it appears as if the entirety of Group III has been searched and that the inclusion of anything less than every claim representing Group III was an error. Thus, **Claims 69-90, 92-99, 101, 102, and 104-106** are pending, and each appears to read on the elected subject matter, i.e. X_6 is O and X_2 is not bound to carbon 3 of the propene chain.

The Restriction Requirement was reiterated in the Office Action dated 10/12/2007 and maintained. The use of the word, "maintained" is confusing since it does not expressly indicate finality. Thus, to clarify, the Restriction Requirement is hereby made final.

Applicant's amendments, filed 01/14/2008, are acknowledged. The rejection put forth under 35 U.S.C. 112, 1st paragraph over **Claims 100-103** is withdrawn.

Claim Rejections

ODP

The ODP rejection made in the Office Action dated 10/12/2007 should have included all claims representing Group III. Thus, the ODP should now include **Claims 69-90, 92-99, 101, 102, and 104-106**. The obviousness-type double patenting rejection put forth in the Office

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Action dated 10/12/2007 is hereby maintained. The newly added claims, **Claims 104-106**, are likewise rejected for the same reasons.

The Examiner would like to apologize for the confusing Applicant (as well as the Examiner) by misconstruing the grouping of the claims both in this rejection and in the Scope of the Subject Matter Searched.

112 – 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 69-73 are rejected under 35 U.S.C. 112, first paragraph, because while the specification is **enabling for compounds of formula (I), optical and geometric isomers, racemates, tautomers, and salts thereof**, it **does not enable hydrates thereof**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In the case *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

Claims 69-73 are drawn to compounds of formula (I), as well as optical and geometric isomers, racemates, tautomers, salts, hydrates, and mixtures thereof. According to Byrn, et al., “the occurrence of hydrated or solvated crystal forms, crystals in which solvent molecules occupy regular positions in the crystal structure, is widespread but *by no means universal among drug substances*.” (emphasis added). Byrn, et al. “Solid State Chemistry of Drugs”, 2d ed., SSCI, Inc., Ch. 10 Polymorphs, pp. 232-247, 232 (1999). Most drug crystals that fall into the category of solvates are hydrates. *Id.* at 236.

While the level of skill in pharmacology and organic chemistry is exceedingly high, there is no absolute predictability as to which solvates and/or hydrates will function as intended. Byrn notes that the water molecule is particularly suited to fill structural voids, due to its small size. *Id.* In hydrated crystal structures, water molecules bind to other water molecules but also to any available functional group, i.e. carbonyls, amines, alcohols, and many others which are capable of accepting or donating an active hydrogen atom to form hydrogen bonds. *Id.* Also, the behavior of hydrates of pharmaceuticals is unpredictable due to dehydration prior to melting, and cracking during dehydration. *Id.* at 234. Too, hydrates and solvates may only be formed under certain conditions, dependent upon the compounds sought to be crystallized. Such a process is not a given in pharmacology and requires a great deal of research, with no guarantee of success.

Furthermore, the stability of solvates and hydrates is not altogether predictable, wherein said stability directly affects the properties of a given molecule. This lack of stability means a hydrate or solvate, if found to possess similar properties as the target compound, may not function as intended *in vivo*. Such facts lead to the conclusion that more than a mere recitation is needed in order to support a claim to solvates and hydrates. Creating functional solvates and

hydrates with the same properties as the mother-compound is by no means routine, thus there must be a showing sufficient to satisfy the enablement requirement.

In the instant case, the Specification provides no guidance as to particular hydrates of formula (I). There are no examples given that Applicant has determined the necessary solvents for even one of the 1000s of compounds encompassed by the genus that is formula (I). There are no determinations as to whether and which hydrates or solvates would function as intended, as useful in the treatment of cerebral ischemia, hemorrhagic stroke, or neuroprotection.

The level of difficulty required to produce functional hydrates and solvates is extremely high. The level of skill in pharmacology/organic chemistry is also very high. However, despite such a high level of skill in the requisite art, the creation of hydrates and solvates is unpredictable to the extent that undue experimentation is required in order to make and use hydrates and solvates of the claimed compounds. There is an insufficient showing in the Specification, or the state of the art does not acknowledge that the hydrates and solvates of the claimed compounds can be created via routine experimentation. Therefore, Applicant's Specification does not enable one of ordinary skill in the art to make and use the invention commensurate in scope with the claims. Applicant may overcome this rejection by deleting "hydrate, hydrate of the salt, or solvate" from the language of **Claims 69-73**.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael P. Barker whose telephone number is (571) 272-4341. The examiner can normally be reached on Monday-Friday 8:00 AM- 5:00 PM. If attempts to

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reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699. The unofficial fax phone for this group are (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is viable through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Michael P Barker/
Examiner, Art Unit 1626

/Rebecca L Anderson/
Primary Examiner, Art Unit 1626